



The Physics of Soft and Biological Matter

P.03 Fluctuating finite element analysis: Modelling biomacromolecules with continuum mechanics

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We present a recently developed, novel method for coarse grained simulation of dynamics of globular proteins. We use a continuum mechanics description of the proteins, solving this using a Finite Element algorithm which we have generalised to include thermal fluctuations, and which is therefore known as Fluctuating Finite Element Analysis (FFEA) [1]. One advantage of this approach is that it permits simulations of molecules those for which no experimental atomistic level structure exists, but for which data is available on the mesoscale shape, and flexibility, of the structure. For example, biophysical techniques that provide such information include cryo-electron microscopy and 3D tomography, which are now sufficiently mature that they merit their own online repository called the EMDataBank (EMDB).

Our method is still in its infancy: we are still developing aspects of the model to include different physical processes. Nevertheless, we have begun to explore biological applications. FFEA has been used to calculate the principal modes of V and A type ATPase membrane motors for comparison with experimental flexibility data, and to produce a quantitative comparison with the results of the Elastic Network Model for the same system. FFEA has also been used to simulate the dynamics of the largest cytoskeletal motor, dynein, in both the APO and ADPVI stages of its power stroke. We have investigated how the crowded environment of the axoneme impedes dynein's thermal fluctuations and the corresponding effect on its exploration of the microtubule surface, allowing us to produce an estimate of the motor's step size *in situ*. We are currently applying the FFEA model to inform the design of biosensors by quantifying how protein flexibility affects binding and unbinding rates from an adhesive surface.

[1] R. Oliver, D. J. Read, O. G. Harlen and S. A. Harris. *J. Comp. Phys.* 2013, 239 147-165